the permeability of the blood-brain and other physiological barriers. Decreasing the degree of tyrosine protein phosphorylation reduces permeability of the blood-brain or other barrier, whereas increasing the degree of tyrosine protein phosphorylation increases permeability.

At page 6, please delete the paragraph appearing at lines 29-32, and substitute therefor the following paragraph:

BRIEF DESCRIPTION OF THE DRAWINGS

FIGURES 1a, 1b and 1c show graphically that pervanadate decreases the transcellular electrical resistance (and by implication increases permeability) of strain I MDCK cells;

At page 9, please delete the paragraph appearing at lines 25-30, and the partial paragraph appearing at lines 32-34, and substitute therefor the following paragraph and partial paragraph:

FIGURE 19 shows a comparison of partial amino acid sequence data obtained for human p100 (SEQ ID NOs:1-5) with corresponding known sequence data from mouse p120 (SEQ ID NOs:1, 6-9). The letters given are based on the standard single letter amino acid code, apart from "X", which indicates any amino acid.

DETAILED DESCRIPTION OF THE INVENTION

In initial experiments, cells were treated with vanadate, a non-selective, but potent, inhibitor of tyrosine phosphatases. In MDCK cells, vanadate alone did not

At page 15, please delete the partial paragraph appearing at lines 15-34, and substitute therefor the following partial paragraph:

To address the issue of the identity of the catenin phosphorylated in response to PAO, peptide-directed antibodies were raised that specifically recognize α- or β-catenin. PAO-treated cells were lysed in SDS, followed by heating to dissociate protein complexes. Under these conditions only individual tyrosine phosphorylated proteins, not proteins associated with tyrosine phosphoproteins, are immunoprecipitated using anti-phosphotyrosine antibody. In such imunoprecipitates, β-catenin is rapidly increased in response to treatment of the cells with either PAO or, as expected, pervanadate (Fig. 6B). However, α-catenin was not detectable in the phosphotyrosine immunoprecipitates (Fig. 6C). Moreover, PAO- or even pervanadate-stimulated tyrosine phosphorylation of α-catenin could not be detected (Fig. 6E) in α-catenin immunoprecipitates (Fig. 6D). Thus, the tyrosine phosphorylation of β-catenin phosphorylation is increased in response to PAO, accounting for its immunoprecipitation by phosphotyrosine antibody. Furthermore, this increased phosphorylation appears to be

At page 17, please delete the partial paragraph that appears at lines 1-17, and substitute therefor the following partial paragraph:

an anti-ZO-1 antibody and tyrosine phosphorylation was examined by immunoblotting. PAO clearly stimulated the tyrosine phosphorylation of ZO-1 and to a lesser extent that of ZO-2 (Fig. 7). Pervanadate clearly resulted in the tyrosine phosphorylation of ZO-1, ZO-2 and, to a much lesser extent, that of a protein of 130 kDa (Fig. 7) possibly the same protein as that

identified by Balda, M.S., Gonzalez-Mariscal, L., Matter, K., Cereijido, M. and Anderson, J.M., 1993, Assembly of the tight junction: the role of diacylglycerol. *J. Cell Biol. 123:293-302.* These data illustrate that tight junction proteins as well as catenins are phosphorylated in response to PAO, raising the possibility that modulation of tight junction permeability could be achieved, either directly or indirectly, via changes in adherens junction adhesiveness and/or by direct modulation of tight junction permeability.

At page 33, please delete the paragraph appearing at lines 20-22 and substitute therefor the following paragraph:

EXAMPLES

The invention will now be illustrated by way of example only. In the following Examples the materials and methods discussed below are utilised.

At page 58, please delete the partial paragraph appearing at lines 3-8 and substitute therefor the following partial paragraph:

followed by heating at 100°C for 5 minutes. Proteins were precipitated by addition of four volumes of ethanol and incubation at -20°C for 16 hours. The precipitate was resolved by SDS-PAGE (6% acrylamide) and proteins were visualized by Coomassie Blue. Protein corresponding to p100 was excised from the gel and digested with LysC. Peptides were separated by HPLC and sequenced (SEQ ID NOs:1-10). Mouse p120 sequence was described by Reynolds et al., 1992. Clearly, human p100 is closed related to mouse p120 (see Fig. 19).